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Frontiers in Clinical Practice of Long-Term Care of Chronic Ventilatory Failure

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Keywords

Chronic respiratory failure · Ventilatory failure · Hypoventilation · Non-invasive ventilation · Mask ventilation · Home mechanical ventilation · Interface · Tracheostoma · Obesity hypoventilation · Muscular dystrophy · Chronic obstructive lung disease

Abstract

Home mechanical ventilation (HMV) is an effective long-term treatment for chronic hypercapnic respiratory failure. In addition to the established practice of providing HMV for the treatment of chronic ventilatory failure in slowly progressive neuromuscular and chest wall disease, there is accumulating evidence for improvement of quality of life and prolongation of survival by HMV in highly prevalent diseases like chronic obstructive pulmonary disease and ever-increasing obesity hypoventilation syndrome as well as rapidly progressive neuromuscular disease. The key concepts for successful HMV are an experienced team selecting the right patients, timely initiation of adequate ventilation via an appropriate interface, and monitoring effectiveness during regular long-term follow-up. Coaching of patients with chronic respiratory failure on long-term HMV within a dedicated service and collaborations with community services for home care are essential. The current review describes various important practical aspects of HMV that remain frontiers in the implementation of the current knowledge in clinical practice and may help in providing effective HMV to all those in need.

Introduction

Home mechanical ventilation (HMV) is an effective long-term treatment that improves quality of life and survival in patients with chronic hypercapnic respiratory failure due to different underlying conditions such as neuromuscular and chest wall disease (NMD/CWD), obesity-related ventilatory failure, and obstructive airway disease [1–3]. The hallmarks of chronic type II respiratory failure (ventilatory failure, failure of the respiratory muscle pump) are chronic hypercapnia (arterial partial pressure of CO_2 [p_aCO_2] >6 kPa) and compensated respiratory acidosis by retention of bicarbonate. Typical findings in addition to the arterial blood gas constellation of chronic respiratory failure during wakefulness are a sleep-associated increase of alveolar hypoventilation, frequent respiratory tract infections, and signs of cor pulmonale and polycythemia.

The most important groups of patients with chronic respiratory failure successfully treated with HMV are patients with obesity hypoventilation syndrome (OHS), pa-

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tients with NMD (e.g., muscular dystrophy or motor neurone disease) or CWD (e.g., kyphoscoliosis), and patients with chronic obstructive pulmonary disease (COPD). However, the cause of alveolar hypoventilation can be found anywhere on the neuromuscular axis from the respiratory centre down to the respiratory muscles, the lungs, or the chest wall.

Positive pressure ventilation is nowadays the standard treatment for chronic respiratory failure. HMV with positive pressure ventilation is either applied non-invasively via a mask or invasively through a tracheostomy. The main goals of mechanical ventilation in chronic respiratory failure are to improve quality of life and to prolong survival. This is achieved by allowing the ventilator to assist the failing respiratory pump in order to provide adequate ventilation and to reduce the work of breathing by unloading the respiratory muscles and improving pulmonary mechanics. To assure effectiveness, optimise patient comfort and patient-ventilator synchrony, and avoid adverse effects, titration and monitoring of mechanical ventilation as well as patient education are essential. A regular follow-up is needed to adapt the ventilator according to the clinical course of the patient's disease and to recognise potential complications. In addition, many underlying conditions that cause chronic respiratory failure are also associated with manifestations in other organ systems or common comorbidities that have to be recognised by physicians treating patients with chronic respiratory failure. Notably, the provision of care and implementation standards for non-invasive ventilation (NIV) services may differ across health care systems and countries. This review outlines practical considerations for HMV in chronic respiratory failure.

Phases of Mechanical Ventilation from Initiation to Long-Term Care

Each phase of long-term mechanical ventilation from initiation of NIV or tracheostomy ventilation over discharge from the hospital into the community to provision of long-term follow-up for HMV is associated with specific challenges. Monitoring of effectiveness of HMV is mandatory in all phases.

The indication to start HMV either arises during regular follow-up in diseases with progressive respiratory muscle weakness (e.g., in NMD) as a consequence of symptoms suggesting respiratory failure in combination with arterial blood gas analysis or a sleep study (with transcutaneous pCO_2 measurement), or during symptomatic acute on chronic respiratory failure as is often the case in COPD and OHS. In COPD, persisting chronic respiratory failure should be demonstrated after an acute exacerbation before initiating long-term HMV [2]. Prognosis of patients with persisting hypercapnic respiratory failure after an acute exacerbation is poor compared to patients with transient hypercapnia or eucapnia [4, 5]. Recent landmark trials in COPD have shown that patient selection for HMV after initiation of NIV during an acute exacerbation of COPD should include a follow-up assessment with arterial blood gas analysis 2–4 weeks after the exacerbation demonstrating persisting hypercapnic respiratory failure [2, 6].

In conditions with expected chronic respiratory failure within the course of disease, HMV should be discussed timely and the patient educated prior to initiation. Initiation of NIV in stable chronic respiratory failure should include titration during physiological monitoring by a specialised team. Adaptation can be performed on the ward or sleep laboratory using respiratory polygraphy or in the high-dependency unit depending on patient needs. The goal is to achieve patient comfort and NIV effectiveness as assessed by correction or reduction of hypercapnia. Elective initiation of NIV usually requires a short in-hospital stay; however, it might be achieved in an outpatient setting in a subgroup of patients [7, 8]. It has been shown that there is no difference in effectiveness of NIV or ventilator usage when NIV is initiated in the outpatient setting in carefully selected, stable patients with NMD/CWD without cognitive impairment or bulbar weakness compared to in-hospital initiation of NIV [7, 8]. Out-patient initiation of NIV in stable patients with chronic hypercapnic respiratory failure and other underlying disease is reality in some centres. However, there is a lack of conclusive trials comparing inpatient and outpatient set-up of HMV. Monitoring serves to demonstrate correction of respiratory failure, to optimise patient-ventilator synchrony, and to avoid overtreatment and adverse effects such as haemodynamic compromise. It also helps to decide whether different day-time and night-time settings might be needed in 24-h HMV. When proven tolerable and effective, an initially close follow-up is recommended, followed by expansion of the intermediate intervals according to the tempo of disease progression and complicating factors. HMV via tracheostomy commonly follows endotracheal invasive mechanical ventilation in the intensive care unit due to acute on chronic respiratory failure and subsequent weaning failure. In an intensive care unit setting, blood gas monitoring by an indwelling arterial catheter is usually given. However, tracheostomy

is sometimes performed electively, e.g., when NIV is no longer applicable due to inadequate bulbar muscle function or when 24-h ventilator support is needed. Titration, monitoring, training (swallowing, speech, de-cuffing, suctioning, etc.) is then usually performed in a high-dependency unit by an interdisciplinary team. Tracheostomy ventilation implicates organising care that guarantees patient security (e.g., special-care home or intensive training of family members). Discharge to rehabilitation or to the community must be planned in advance.

Patient Selection

Depending on the aetiology of chronic respiratory failure, criteria for patient selection for HMV and the interface used differ.

Obesity Hypoventilation Syndrome

OHS, chronic hypercapnic respiratory failure due to obesity with or without associated obstructive sleep apnoea syndrome (OSAS), is the most common indication for HMV in many countries. Positive pressure ventilation is indicated in patients with OHS at the time of diagnosis to improve respiratory mechanics, adjust neural respiratory drive, and keep the upper airway patent during sleep. HMV can usually be applied non-invasively. However, HMV is commonly initiated within the course of emergency hospitalisations due to acute on chronic respiratory failure in OHS, and patients may be difficult to wean from invasive mechanical ventilation. Although both CPAP and NIV have been shown to correct respiratory failure [9–11], NIV is superior to CPAP in improving exercise capacity and pulmonary hypertension [12]. The degree of sleep hypoventilation and apnoeas or hypopnoeas contributing to hypercapnia differs across the spectrum of OHS/OSAS, and the dominating underlying sleep-disordered breathing may guide the choice of initial positive pressure ventilation. CPAP is easier to implement and less expensive, and both CPAP and NIV have been shown to improve gas exchange. If NIV is needed to effectively control hypoventilation in the initiation phase, a down-step to CPAP might be possible after a few weeks or months [13]. The indication for HMV as treatment for chronic respiratory failure should be re-evaluated after substantial weight loss, e.g., in response to bariatric surgery [14–16].

OHS patients often need relatively high expiratory positive airway pressure (EPAP, 8–14 cmH_2O) to guarantee upper airway patency, and additional pressure support to correct hypoventilation: the back-up rate can be set quite high (14–18/min). Additional supplementary oxygen is sometimes needed in the initial phase of ventilation, but usually unnecessary with an effective ventilator setting and in the absence of pulmonary comorbidity.

Neuromuscular and Chest Wall Disease

NIV is usually initiated for symptomatic chronic alveolar hypoventilation, but several parameters are monitored proactively during regular follow-up to assess progressive respiratory muscular weakness and to detect looming ventilatory failure in patients with slowly progressive NMD/CWD, e.g., forced vital capacity (FVC), maximum inspiratory and expiratory pressures, peak cough flow, arterial oxygen saturation, and carbon dioxide partial pressure every 6–12 months in adult patients with muscular dystrophy type Duchenne [17, 18]. Since ambulation has usually been lost previously in NMD, decline in FVC and respiratory failure might occur with very few symptoms (e.g., no exercise dyspnoea). FVC is an important predictor of respiratory failure, e.g., FVC <50% makes ventilatory failure likely. In patients with deformities of the vertebral spine and chest wall, the percent predicted of FVC should be calculated based on the arm span [19]. Non-invasive respiratory muscle strength testing (sniff nasal inspiratory pressure, maximal inspiratory pressure, and maximal expiratory pressure) is also useful in predicting respiratory failure [20–22]. Ineffective cough, recurrent lower respiratory tract infections, and hypoventilation associated with right heart failure are the leading causes of morbidity and mortality in NMD. An anticipatory monitoring approach allows timely initiation of cough assist, nocturnal, and subsequent daytime ventilatory support [23]. In patients with muscular dystrophy type Duchenne, HMV should be discussed and initiated when symptomatic nocturnal hypoventilation or advanced respiratory muscle weakness develops (FVC or maximal inspiratory pressure fall below 50% or 60 cmH_2O, respectively) [24]. These patients are at risk for daytime ventilatory failure at short or intermediate term [25]. NIV usage is usually extended from night-time into day-time. It can even be extended to 24-h usage in combination with airway clearance techniques so that tracheostomy can be avoided. Survival and quality of life benefits due to HMV have been demonstrated in several studies in patients with muscular dystrophy [26] and CWD [18] and recently also in patients with motor neurone disease (also non-invasively when bulbar function is sufficient) [27–29]. In patients with rapidly progressive NMD such as bulbar and respiratory forms of amyotrophic lateral sclerosis, for example,

assisted ventilation via a mask is generally preferred, and tracheostomy is rarely recommended to avoid the development of a locked-in state and associated suffering during the final stages of life. Although there are very few randomised controlled trials, HMV has found a widespread application in patients with NMD/CWD.

Chronic Obstructive Pulmonary Disease

Chronic hypercapnia in patients with COPD is associated with a particularly bad outcome with a high mortality and frequent hospitalisations. Patient selection and the correct ventilation strategy is crucial in COPD. Evidence for benefit on hospital admission-free survival and quality of life in COPD is accumulating since the introduction of high-intensity NIV aiming at normalising p_aCO_2 [2, 30, 31]. In addition, EPAP has to be titrated high enough to overcome intrinsic positive airway pressure and its inspiratory threshold load, but a too high EPAP may aggravate hyperinflation. Patient-ventilator asynchronies are common in COPD and should be considered during set-up. Overall, titrating NIV in COPD needs time and monitoring. COPD patients usually need a much higher pressure support than NMD or obesity-related respiratory failure. COPD patients usually also require additional long-term oxygen to HMV to address both the gas exchange problem and ventilatory failure. HMV is typically applied non-invasively during sleep and extended into the daytime as needed. However, some patients who cannot be weaned after intubation and mechanical ventilation after acute on chronic respiratory failure might be ventilated via tracheostomy. Patient selection criteria for HMV in COPD have recently been established: clinicians should reassess post-acute NIV COPD patients 2–4 weeks after clinical recovery; if the p_aCO_2 remains >7 kPa, NIV should be considered [2]. However, NIV should also be discussed in stable patients with slowly progressive hypercapnia on optimal medical treatment without a history of NIV during an acute exacerbation of COPD (chronic vs. acute on chronic hypercapnic respiratory failure). The credo is: select the right patients and ventilate adequately. However, treating COPD patients with long-term NIV needs time, experience, and a dedicated infrastructure.

Interfaces

Initiation of HMV starts with the choice of the appropriate interface. NIV via an oro-nasal or nasal mask has several advantages over invasive ventilation. In particular, mask ventilation allows for convenient, intermittent use during sleep or resting periods, or as needed otherwise. The opportunity to speak and eat/drink during natural breathing and to be free of any technical support during daytime hours and social interactions is very important to many patients as it allows them to avoid the stigma of appearing to be handicapped. Invasive HMV via a tracheostoma may be preferable for patients with large amounts of secretions that require endotracheal/bronchial suctioning and for those with a need for continuous 24-h ventilatory support (see below). However, large amounts of secretions may also complicate tracheostomy ventilation, especially in patients with bronchiectasis.

Interfaces for NIV

The choice of the right interface is required for successful NIV. The mask is a key factor for patient comfort and adherence to therapy and therefore long-term success of NIV. Oro-nasal (full-face) interfaces are usually the first choice when starting NIV because many patients with decompensated chronic hypercapnic respiratory failure tend to breathe through their mouth. It is recommended to test several masks for patient comfort and effectiveness. Oro-nasal masks, nasal masks, and nasal pillows are most often used in long-term HMV (Fig. 1). Oro-nasal masks are usually associated with lower leakage during sleep. Nasal masks or pillows may be better tolerated during daytime, especially in 24-h ventilator dependency, as generally patients learn to speak and swallow even during application of NIV. When choosing interfaces, it is always necessary to check the compatibility of the mask with the ventilator circuit, e.g., an open single-limb circuit requires leak orifices in a vented mask or in the circuit to prevent CO_2 rebreathing. The manual skills of the patient should also be appropriately considered in the selection of the mask since some models are more challenging to apply or more fragile than others (Fig. 1). Regular check and replacement of the interfaces is important during HMV. Availability of different masks may be useful in case of pressure ulcers and other mask-related side effects. Mask fitting and practice in handling may help to reduce local side effects and air leaks. It is necessary to regularly reassess mask fit and air leaks during treatment (straps tend to loosen). Nowadays, a less common interface for NIV than masks is a mouthpiece (Fig. 1). Mouthpiece ventilation might be used part-time during daytime in the wheelchair in patients with NMD if better tolerated and considered safe (e.g., good mouth closure and function-

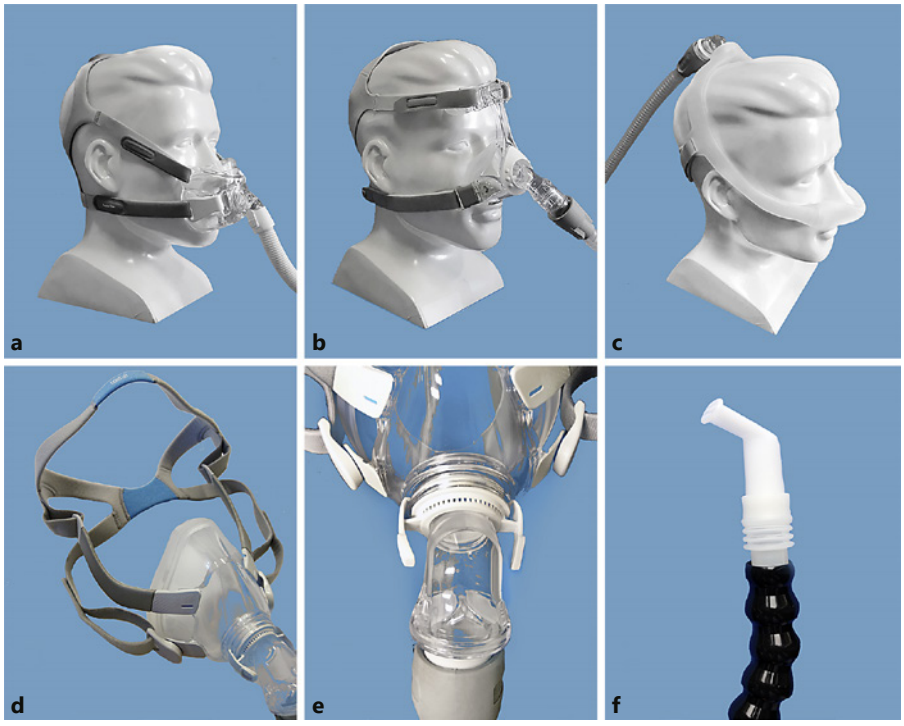

Fig. 1. Examples of masks for NIV: oro-nasal (**a**, **d**) and nasal masks (**b**, **c**), and detailed view of leak orifices and safety valve of an oro-nasal mask (**e**) and an angled mouthpiece (**f**).

ing neck movements) [32]. Many ventilators provide a specific mode for mouthpiece ventilation. Its advantages over NIV by a mask are mainly the opportunity for intermittent use as needed by patients who are unable to put on a mask themselves. Furthermore, mouthpiece ventilation during daytime might facilitate speaking and eating [32].

Interfaces for HMV via Tracheostomy

Only a small proportion of patients receives HMV via tracheostomy [33]. Patients with spinal cord injuries and NMD build the largest groups. An advantage is the possibility for airway suctioning and the prevention of air leakage (when cuff inflated) while still allowing speech when the cuff is deflated and a one-way valve (Passy-Muir or similar valve) set in place. There are different cannulas available (e.g., cuffed, uncuffed, rigid, flexible, inner/outer tube, speaking valve) (Fig. 2). The choice of the right tracheostomy tube length and diameter is important. A cuffed tube seals the airway; however, it has several disadvantages, e.g., renders the patient unaccustomed to swallowing and can cause damage to the tracheal wall (cuff pressure has to be monitored). While necessary in the acute phase of a tracheostomy, a continuously inflated cuff is often not necessary in stable long-term HMV. Tracheostomy is associated with specific possible complications such as life-threatening bleeding, ventilator-associated pneumonia, mucus plugging, or tracheal granuloma formation and stenosis.

Selection of the Ventilator Circuit and Settings

When selecting the specific type of ventilator for a particular patient one should consider the degree of dependency (full ventilatory dependency, intermittent ventilatory use, need for battery powered operation), NIV or invasive ventilation, the required pressure range, physical impairment, comorbidities and mobility of the patient, as well as know-how and preferences of the local care team.

For mask HMV in patients requiring only intermittent support, a single-limb vented circuit is usually selected. It needs exhalation orifices in the mask (Fig. 1), in a connector between the mask and the tube, or the distal circuit to prevent rebreathing [34]. A one-way valve is mounted just before or in the mask for safety reasons assuring spontaneous breathing in case of ventilatory failure. Rebreathing in a vented single limb circuit is affected by the size of the orifices and the EPAP. In mask ventilation, tidal volume and applied minute ventilation cannot be precisely estimated, and setting alarms on these variables are therefore not routinely performed and are not reliable.

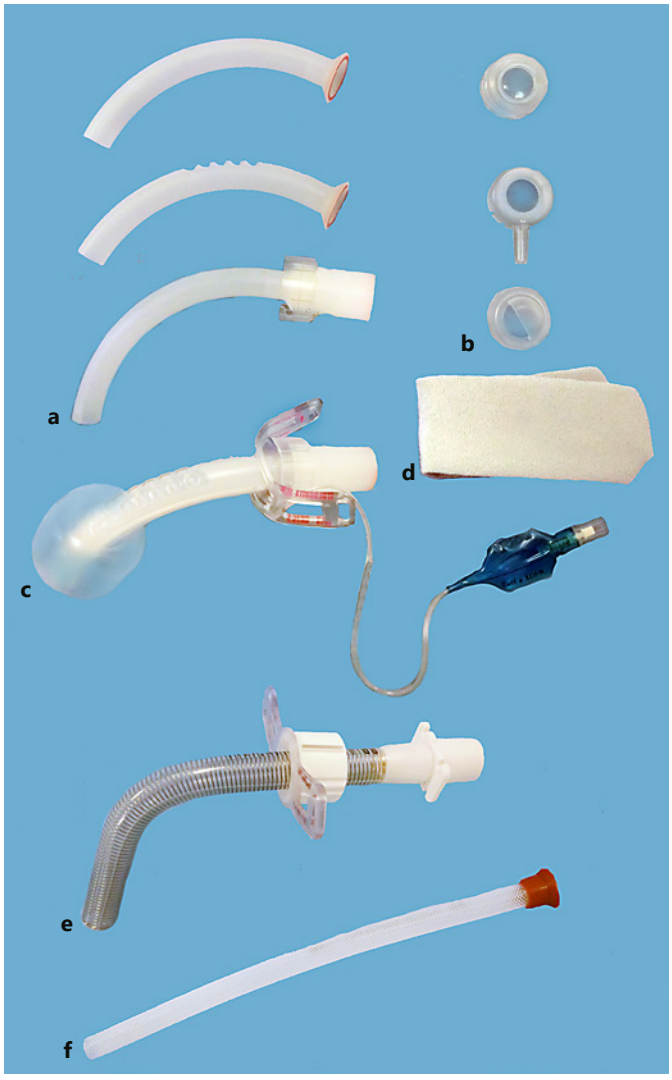

Fig. 2. Tracheal cannulae. **a** Three types of rigid inner cannulae fenestrated and non-fenestrated. **b** Speaking valve and cover pieces for room air breathing and oxygen administration. **c** Fenestrated, cuffed tracheal cannula, with fixation band (**d**). **e** Flexible, uncuffed cannula, with its inner tube (**f**).

A single-limb non-vented circuit has an exhalation valve controlled by the ventilator at the distal end of the circuit [35]. A double-limb circuit consists of an inspiratory and expiratory limb (Fig. 3). These are connected to the ventilator via non-rebreathing valves, and to the interface via a Y-piece. Non-vented circuits with valves are commonly used for invasive ventilation. A double-limb system allows for precise estimation of administered and exhaled tidal volume and minute ventilation and for the detection of unintended leaks. In addition, various alarms can be set for life-supporting ventilation.

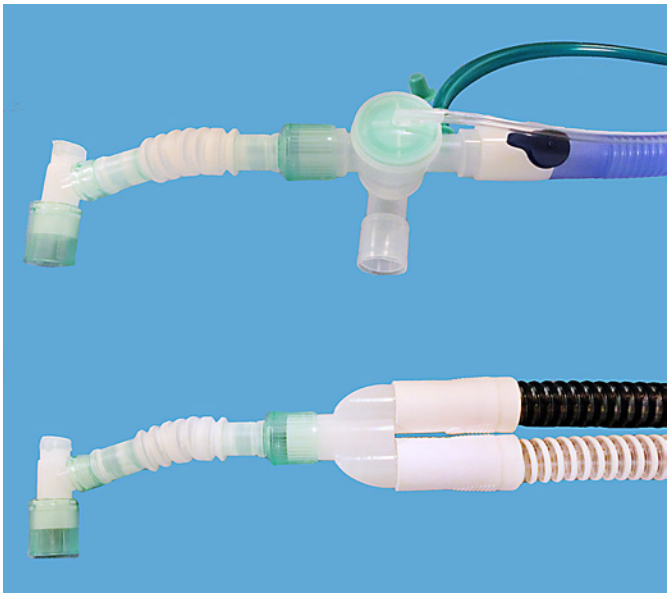

Fig. 3. Ventilator circuits. Upper part: single-limb circuit with exhalation valve; lower part: double-limb circuit.

Ventilator Mode and Settings

Table 1 summarises the main modes and settings used during HMV. The selection is guided by the underlying disease and dependency, but individual adjustments are required for optimal efficacy and comfort.

Bi-Level Pressure Support Ventilation

Bi-level pressure support ventilation (BiPAP, PSV) – most often spontaneous-timed (ST) mode with a minimal back-up rate – is the most frequently used mode in HMV according to a European survey [36]. Individually different levels of pressure support (inspiratory positive airway pressure [IPAP] minus EPAP) will be necessary to correct alveolar hypoventilation. Tidal volume increases nearly linearly with increasing pressure support. Pressure support is commonly limited by leak and patient discomfort above 25–30 cmH_2O in case of NIV. Based on the mode, ventilation will be controlled (timed mode, T), assisted (spontaneous mode, S) or both (ST). In pressure support ventilation, optimal EPAP, trigger sensitivity, pressurisation (rise time of pressure support), IPAP or level of pressure support, and cycle-off (expiratory trigger sensitivity) have to be titrated. EPAP is titrated to keep the upper airway open and/or to overcome intrinsic positive end-expiratory airway pressure (PEEP) to improve pulmonary mechanics and reduce the work of breathing depending on the underlying pathophysiology of ventila-

Table 1. Ventilator modes and settings commonly used in HMV

Abbreviation	Mode	Settings*
CPAP	Continuous positive airway pressure	CPAP, maintained through all phases of the breathing cycle
PSV-S	Pressure support ventilation, spontaneous mode	IPAP, EPAP, TImin, TImax, inspiratory and expiratory (cycle) trigger sensitivity, inspiratory rise time
PSV-ST	Pressure support ventilation, spontaneous/timed mode	IPAP, EPAP, respiratory frequency, TImin, TImax, inspiratory and expiratory (cycle) trigger sensitivity, inspiratory rise time, expiratory pressure decrease speed (cycle-off)
PSV-T	Pressure support ventilation, timed mode	IPAP, EPAP, respiratory frequency, TI, inspiratory rise time, expiratory pressure decrease speed, cycle-off
(a)PCV	(assisted) Pressure control ventilation	IPAP, EPAP, respiratory frequency, TI (TI:TE), inspiratory trigger sensitivity, inspiratory rise time, expiratory pressure decrease speed
VAPS/AVAPS and tri-level PAP	(average) Volume-assured pressure support ventilation and variable inspiratory/expiratory positive pressure ventilation	EPAP fixed or variable (autoEPAP), variable pressure support with PS min, PS max, target volume, TImin, TImax, inspiratory and expiratory (cycle) trigger sensitivity, inspiratory rise time, expiratory pressure decrease speed, cycle-off

* Any particular setting may not be available in all ventilators, depending on brand. IPAP, inspiratory positive airway pressure; EPAP, expiratory positive airway pressure; TImin, minimal inspiratory time; TImax, maximal inspiratory time; TI, inspiratory time; TE, expiratory time.

tory failure. EPAP also improves functional residual capacity and ventilation-perfusion matching. Ventilation should aim at normalising or reducing p_aCO_2 and at a tidal volume of 7–9 mL/kg ideal body weight [30]. However, tidal volume is often under- or overestimated by ventilator software, especially in the presence of unintentional leaks. Trigger sensitivity (flow-dependent > pressure-dependent > complex algorithms) should be chosen to avoid excessive work of breathing, wasted efforts, and auto-triggering/cycling. A shorter rise time is needed in obstructive airway disease compared to restrictive airway disease for a suitable inspiration to expiration ratio, but has also to be titrated according to patient comfort. Cycle-off criteria should be chosen to match the duration of inspiration with the neural inspiratory time and should also consider patient comfort. Cycling-off at a higher percentage of peak inspiratory flow (percentage of peak inspiratory flow is a commonly used cycling-off criterion) is chosen in COPD compared to NMD/CWD. The presence of air leaks may interfere with flow-cycling. Most ventilators allow setting a minimal and maximal inspiration time to set a safety limit for the cycling window.

Pressure-Controlled Non-Invasive Ventilation

Pressure-controlled non-invasive ventilation is the second most often used mode and has a fixed inspiratory time (whereas there is a cycle-off criterion and a maximum inspiratory time in bi-level pressure support ventilation).

Volume-Targeted Modes

Volume-targeted modes have recently been used. A hybrid mode providing an assured tidal volume during pressure support ventilation has become available (e.g., VAPS/volume-assured pressure support or AVAPS/average volume-assured pressure support). IPAP is adapted within pressure support or pressure-controlled modes to guarantee a pre-set averaged tidal volume (usually around 6–8 mL/kg of ideal body weight). However, there is currently no evidence for a superiority of (A)VAPS over bi-level pressure support ventilation in specific settings. In addition, these modes have certain pitfalls such as a loss of pressure support in case of a higher than targeted tidal volume, or the fall or increase of pressure support in the presence of unintentional leaks depending on the circuit.

Volume-Controlled Ventilation and Intermittent Positive Pressure Ventilation

Volume-controlled ventilation and intermittent positive pressure ventilation are seldom used in HMV. Volume-controlled ventilation may have more gastrointestinal side effects due to the changes in IPAP.

Tri-Level NIV

Tri-level NIV is a term used for a combined bi-level positive pressure ventilation mode that provides fixed or variable inspiratory pressure support according to the modes described above and applies a variable, auto-adjusted EPAP similar to autoCPAP used to treat OSA. This combined mode may be advantageous in selected patients with OHS/OSA or other forms of combined hypoventilation and obstructive or central sleep apnoea, but no scientific evidence is available to date to demonstrate its superiority over standard NIV modes [37].

Humidification and Additional Support

Not every patient on NIV requires additional humidification since breathing through the nose assures warming and humidification of the inspired air like during natural breathing. Dryness of the nose and mouth and excessive nasal secretion may reflect oral leaks during nasal ventilation or mouth breathing. In these cases, the use of an oro-nasal (full-face) mask is advisable. Alternatively, or in addition, a passive humidifier may provide additional comfort. In invasive HMV via a tracheostomy tube, heated humidification is advisable to prevent drying out of the central airways which can result in dangerous airway obstruction through tedious secretions and mucus plugs. Some patients on HMV via tracheostomy use humidification only when stationary but have a wheel-chair mounted ventilator without humidifier to prevent motion-induced water accumulation in the circuit when driving around.

Patients with underlying diseases with impaired gas exchange may need the addition of long-term oxygen therapy to HMV. Most ventilators for HMV have a dedicated, low-pressure oxygen inlet. It shuts off automatically in case of interruption of ventilation in order to avoid fire hazard from high oxygen concentrations accumulating within the ventilator. High-pressure/flow oxygen supplementation is not generally available in the home care setting.

Besides treating chronic respiratory failure, the respiratory physician caring for patients on HMV should also be aware of, monitor, and treat comorbidities and other manifestations of specific diseases (e.g., in NMD) unrelated to or interfering with effective NIV.

Mobilisation of secretion should be assisted by coughing techniques, postural drainage, physiotherapy, and in advanced respiratory muscle weakness with ineffective cough, by an exsufflation-insufflation device (cough assist). A cough assist, providing mechanical insufflation-exsufflation to support airway clearance, is commonly prescribed to prevent atelectasis and pneumonia in patients with NMD when peak cough flow is lower than <270 L/min (4.5 L/s) [23, 38–40]. The peak cough flow thresholds of 270 L/min and 160 L/min have been shown to predict inability to cough to effectively clear airway secretions and chronic respiratory failure, respectively [38, 41]. An experienced physiotherapist is needed to instruct and assist the patient in the use of a cough assist.

A percutaneous endoscopy gastrostomy is indicated in patients with impaired swallowing to avoid respiratory complications and to allow for sufficient administration of fluid and nutrition without stressing the patient. In patients on HMV, it has been shown to be beneficial to place a percutaneous endoscopy gastrostomy with a gastric and intestinal tube. The gastric tube allows deflation in case of aerophagia, which is a common side effect of positive pressure ventilation.

Especially in NMD and in paraplegic patients, administration of sufficient fluids, properistaltic agents, and laxative drugs are essential to avoid constipation and more severe abdominal complications as consequences of the disturbed gastrointestinal motions [42].

Monitoring

Monitoring of NIV focuses on improving patient-ventilator synchrony and reducing leakage, besides maximising effectiveness in terms of correcting respiratory failure and sleep-disordered breathing. Optimising settings by monitoring physiological parameters will improve patient comfort and adherence to long-term NIV. Monitoring options are clinical and haemodynamic parameters, arterial blood gas analysis, pulse oximetry, transcutaneous pCO_2, respiratory polygraphy (with the possibility of comparing respiratory effort and ventilator-provided support), and ventilator-dependent information on timing, triggering, pressure, flow, and volume. The choice of monitoring facilities depends on the setting and complexity of the patient's condition; however, a minimum of monitoring to guarantee effectiveness and tolerability is always necessary.

Arterial Blood Gas Analysis

Arterial blood gas is a very common tool used to assess both ventilation and oxygenation as well as gas exchange by measurement of the pH and arterial partial pressure of CO_2 and O_2 (p_aCO_2, p_aO_2) and calculated parameters (e.g., alveolo-arterial pO_2 gradient, base excess). Its re-

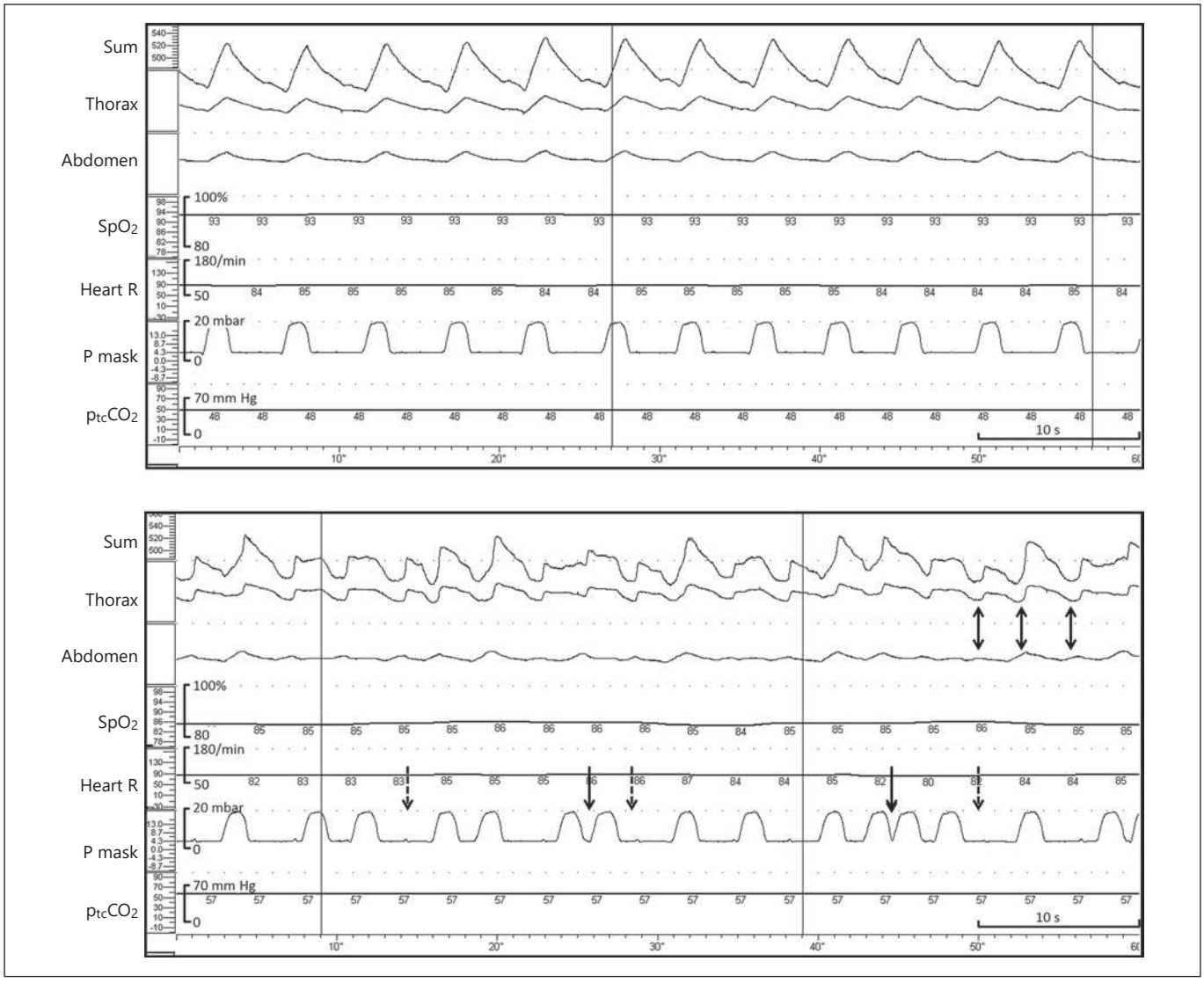

Fig. 4. Polygraphic recordings during initial adaptation of mask ventilation in a patient with chronic hypercapnic respiratory failure due to chronic obstructive pulmonary disease. The time series show 60-s periods of chest wall excursions by inductive plethysmography, pulse oximetry (SpO_2), pulse rate, mask pressure, and transcutaneous capnography ($p_{tc}CO_2$). In the upper panel, there is near perfect synchronisation of the chest wall motion with the ventilator. In the lower panel, there is patient/ventilator asynchrony with irregular breathing, paradoxical chest wall excursions (double arrows), trigger failure (arrows with broken lines), and inadequate triggering (arrows with solid lines). Patient-ventilator asynchrony results in inefficient ventilation with an increase in $p_{tc}CO_2$ and a drop in SpO_2. Heart R, heart rate; P mask, mask pressure.

sults are rapidly available and allow prompt decision making and adaptation of ventilator parameters. It is the gold standard to assess ventilation.

Transcutaneous Capnometry

Transcutaneous monitoring of carbon dioxide ($p_{tc}CO_2$) is a valid method to non-invasively and continuously monitor changes of $p_{tc}CO_2$ during NIV [43]. The level of agreement with p_aCO_2 is acceptable and the great advantage is the possibility to monitor trends over time non-invasively [44].

Polysomnography and Respiratory Polygraphy

A more pragmatic approach than polysomnography is respiratory polygraphy combined with transcutaneous pCO_2 measurement (Fig. 4). Monitoring of chest

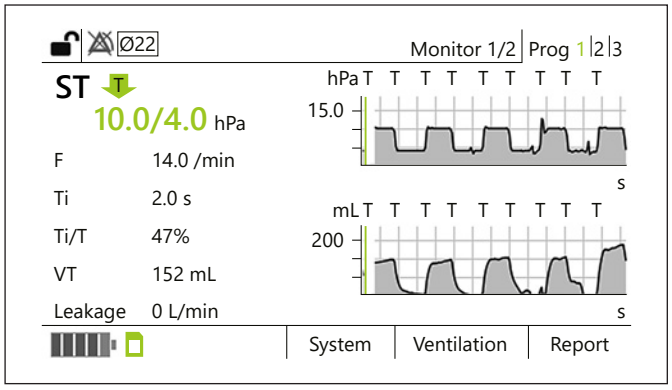

Fig. 5. Ventilator display showing pressure and volume curves in real-time along with numerical information on timing, applied volume, and pressure.

wall motion by respiratory inductance plethysmography together with ventilator-derived pressure and flow as well as pulse oximetry and capnometry allows titration and optimisation of HMV based on physiologic monitoring. Advanced physiologic monitoring such as electromyography of respiratory muscles or oesophageal pressure has provided physiological insights but has not been implicated in routine clinical practice so far.

Ventilator Curves

Several ventilators allow real-time graphical visualisation of variables (Fig. 5) such as volume, pressure, and flow over time (time series curves) or the interaction between two variables over the course of a breath (loop). This can provide information on whether breaths are spontaneously triggered (started) and cycled (stopped) or mandatory (when they are triggered or cycled or both by the ventilator).

Ventilator Software Data Chip

Downloading and checking ventilator software statistics that usually provide information on setting, usage, tidal volume, minute ventilation, pressures, spontaneous and machine triggered breaths, and leakage is especially helpful to adjust settings and encourage the patient during follow-up of HMV (Fig. 6). Large unintentional leaks my lead to side effects such as sleep fragmentation and patient-ventilator asynchrony, and to insufficient ventilation although pressure support ventilation may compensate for unintentional leaks [45, 46]. Thresholds for high measured leaks depend on the ventilator and the interface and have not been established by convincing evidence. Moreover, rapid changes in leaks seem to be more relevant than absolute values of leak flow in terms of patient disturbance. In any case of an excessive and highly variable leak, interface fitting and handling by the patient must to be evaluated. Chin straps might be helpful with a nasal interface [47]. Humidification may reduce nasal resistance [48].

Telemedicine

The role of telemedicine in improving adherence and settings, and thereby patient outcomes, is not yet clear [49, 50]. Although most current ventilators used for HMV can be interfaced with pulse oximetry to monitor oxygenation, transcutaneous self-monitoring of carbon dioxide in the patient's home is not practically feasible due to the technically challenging application and high cost of the capnography device sensor. This imposes an important limitation to telemonitoring of patients on HMV. In theory, telemonitoring offers a potential for better use of resources and faster intervention in case of insufficient usage, clinical deterioration, or sub-optimal ventilator setting, and awareness of this option will increase. Different monitoring parameters like applied pressure, breathing pattern, estimated ventilation, pulse oximetry, and built-in software information are available via telemonitoring. However, standards on how to use telemonitoring as part of an HMV service and clear evidence on its benefit are not yet available. Figure 7 shows a suggested simplified algorithm for monitoring levels of HMV during sleep and wakefulness.

HMV Service and Follow-Up

It has to be highlighted that the right setting is important for successful HMV. The facilities and opportunities may vary among health care systems and countries. HMV is most successful if performed comprehensively in a collaborative team comprising the patient and his/her family, home care personnel (either from the community, a non-profit organisation such as the Lung Ligue, or a commercial company), a family physician, and professionals from various services including respiratory medicine, cardiology, gastroenterology, nutritional support, neurology, and others depending on specific problems. A regular exchange of essential information between the patient and the different care givers is important. Adequate facilities with experience in the im-

Fig. 6. Graphical display of data downloaded from the ventilator during HMV in a patient with chronic obstructive pulmonary disease. The upper panel shows the daily hours of use (8:54 h on average) and the set inspiratory and expiratory pressures in BiPAP ST mode over the course of 4 months. The lower panels show detailed data from one night (9 h) during this period. This information helps to verify optimal efficacy and use during long-term HMV.

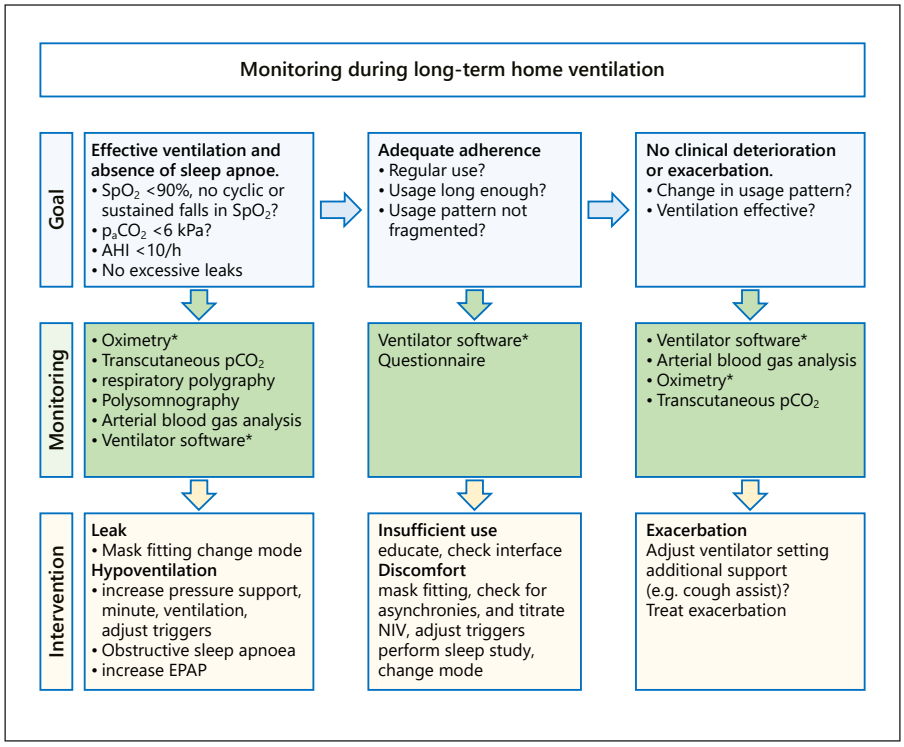

Fig. 7. A simplified algorithm on monitoring of HMV in chronic ventilatory failure. Different goals, suggested monitoring tools, and possible interventions are shown. * Monitoring via telemedicine possible.

plementation of HMV and long-term support are mandatory. A dedicated setting should include an outpatient and inpatient clinic, a sleep laboratory, and a high-dependency unit with specialised medical and paramedical personnel and equipment. Access to an emergency room and intensive care unit should be readily available. Regular follow-up of patients treated with HMV is essential to ensure that HMV is effective, the patient is using it appropriately, and the equipment is functional [51]. In general, an outpatient follow-up in an NIV service is required at least yearly; however, depending on the course of the disease and episodes of acute on chronic respiratory failure, a closer follow-up is needed, especially in the initiation phase.

Disease- and Ventilator-Specific Problems

The forms and modes of ventilation as well as the underlying disease causing chronic respiratory failure harbour specific risks associated with HMV. Some examples are given.

Invasive ventilation via tracheostomy may result in bleeding from the tracheostomy side, cuff-induced tracheal ulcers or stenosis, speech problems, airway obstruction by secretion, and ventilator-associated pneumonia, whereas NIV involves the risk of local interface side effects (such as ulcers) and leakage.

Intercurrent lower respiratory tract infections with aggravated airway secretions can result in acute on chronic ventilatory failure on HMV and make intubation necessary. Intercurrent respiratory tract infections and reduction of fluid and food intake make the patient prone to life-threatening metabolic derangements [52]. Specialist chest physiotherapy and cough assist might be used to prevent mucus plugging and atelectasis.

Bulbar dysfunction in NMD increases the risk of aspiration, which can be assessed by a swallowing test. Gastrostomy can be used as an alternative feeding method; however, there is still the risk of aspiration of oral secretions.

COPD predisposes to patient-ventilator asynchrony. Therefore, monitoring of respiratory effort and patient-ventilator synchrony during initiation and titration of NIV is of great importance in these patients.

Future Developments and Outlook

There are continuously ongoing developments in patient interfaces that will enhance the comfort and effectiveness of NIV. Novel ventilator modes that automati-

cally adjust settings ("smart" ventilators) to assure a target minute volume or a minimum tidal volume and that adjust to physiologic changes during changes in sleep stages and positions are likely to be used more. However, benefits and harms of these novel modes have to be scientifically evaluated first, and it will always remain important that an experienced person is setting the ventilator up. In addition, high flow devices might be used in specific subgroups, although the implementation of this outside the hospital (home high flow) might be difficult to realise, and the place for high flow therapy is more likely in acute than in chronic respiratory failure. Telemedicine is increasingly available, but standards for data handling are not defined. Before its implementation in NIV services, it needs to be demonstrated that telemedicine improves patient outcomes or reduces hospitalisations [49].

In summary, HMV has the potential to improve various clinical and physiological outcomes. It may reduce work of breathing and metabolic demand, increase tidal volume, and reduce p_aCO_2. This may reset the deranged chemoreceptors, as well as improve respiratory mechanics, prevent atelectasis, and improve ventilation/perfusion matching. Monitoring is needed to improve and reassure these outcomes and to avoid adverse effects, unintentional leaks, and patient-ventilator asynchrony. Regular assessment of the effectiveness of HMV is recommended during follow-up, depending on the course of the underlying cause of chronic respiratory failure, usually by daytime arterial blood gas analysis and nocturnal capnography and pulse oximetry.

Conclusions

The key concepts to successful HMV are an experienced team selecting the right patients, initiating NIV timely, and following up patients with chronic respiratory failure regularly in a dedicated interdisciplinary service. Possible extra-pulmonary manifestations of the underlying disease and comorbidities should always be kept in mind. Optimal access to HMV and follow-up in specialised centres for HMV for the large group of patients with an indication of and benefit from HMV are essential.

The frontiers remain the implementation of the current knowledge in clinical practice and providing HMV according to current standards to all those in need.

Disclosure Statement

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Author Contributions

E.I.S. and K.E.B. were responsible for the conception and design of the study. E.I.S. was responsible for drafting the article.

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